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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,295	09/11/2003	Wolf-Ruediger Schaebitz	242650US0CONT	6092

22850 7590 11/10/2008

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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
11/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/659,295	SCHAEBITZ ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/24/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,9,11-14,16-19 and 105-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,9,11-14,16-19 and 105-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/7/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 13, 17-19, and 105-112 have been amended as requested in the amendment filed on July 24, 2008. Following the amendment, claims 1, 5-7, 9, 11-14, 16-19, 105-112 are pending and are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on July 24, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 11 and 13 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reasons of record in the Paper filed May 22, 2008.

6. Claim 11 stands as indefinite in its recitation of a "hemodynamically active compound" as a limitation. On page 8 of Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that hemodynamic is a well-known term in the field and whether a compound does this or not can easily be ascertained by one in the field. Examiner maintains that while "hemodynamic" may be well known the distinguishing features of a hemodynamically active compound are unclear. Therefore,

the metes and bounds of encompassed compounds are indefinite and an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter.

7. The term "facilitates" in claim 13 stands as indefinite for being a relative term. On page 9 of Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that facilitates has a well-defined term “to make easier or less difficult" and states "the agent here makes it easier or less difficult for GCSF to pass through the blood brain barrier". While this has been considered it is not found persuasive because the indefiniteness arises not from the plain meaning of the term “facilitate” but rather that the claim does not provide requisite degree for the facilitation, or the degree to which the agent makes GCSF pass the BBB more easily. One of skill in the art would not know with which to compare the ease of passage across the BBB and therefore the metes and bounds of the invention are indefinite.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. As currently amended, Claims 1, 9 and 18 stand as rejected under 35 U.S.C. 102(b) as being anticipated by Heard *et al*. (2004) as evidenced by NCBI protein

accession number P09919 (1989), for reasons of record in the Office action mailed May 22, 2008.

10. On pages 6-8 of Remarks filed July 24, 2008, Applicant traverses the rejection on the following grounds: (1) Heard et al. does not teach treating traumatic brain injury (TBI) but rather teaches "the prophylactic treatment of 'nosocomial infections in intubated patients with acute TBI or intracerebral hemorrhage'" (page 6 Remarks, citing pg. 749, column 1, paragraph 2 of Heard reference); and (2) Heard does not inherently teach treating TBI because "something that is inherent must inevitably be the result each and every time" and Examiner has not provided evidence or scientific reasoning to establish the reasonableness of inherency(Remarks, page 7). Applicant states that Heard does not present beneficial effects of GCSF in TBI patients. While these arguments have been considered in full they are not found persuasive to overcome the rejection for the following reasons.

11. Claims are drawn to a method of treating traumatic brain injury (TBI) in a mammal comprising administering mammalian and/or human G-CSF. The Heard et al. prior art teaches a method comprising administering human G-CSF to 20 human patients with acute traumatic brain injury or cerebral hemorrhage comprising administering recombinant human G-CSF (brand name Filgrastim, 100% identical to that of SEQ ID NO: 28 of the instant specification) and demonstrate that filgrastim alleviates one TBI-associated symptoms (bacteremia).

12. Examiner reiterates the evidence and reasoning as set forth in the previous Office action. Briefly, the method of the instant claims does not distinguish in any way

over the method of the prior art because the claims neither call for a specific feature by which to limit the patient pool of TBI patients, nor do the claims stipulate specific criteria by which "treatment" of TBI is assessed. Therefore, Applicant's argument that inherency must demonstrate some result each and every time is not persuasive because the instant claims do not recite a requisite result as a limitation. The claim comprises one active step, administering mammalian/human G-CSF to a mammal/human patient with traumatic brain injury. While Heard does not distinguish the ratios of patients with TBI versus those with intracerebral hemorrhage, however, it does teach administration to patients with TBI or hemorrhage. Thus, in so far as the Heard reference describes administration of Filgrastim to even one TBI patient, it fully anticipates the method of the claims. Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 5-7 stand as rejected under 35 U.S.C. 103(a) as being unpatentable over Heard et al. as applied to claims 1, 9 and 18 above, and further in view of Brines et al. (2000) for reasons of record in the previous Office action mailed May 22, 2008.

On page 8 or Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that because the primary reference, Heard, is silent about treating the underlying condition of TBI, then each of the combinations subsequently fail.

In above sections 10-12 of the instant office action Examiner provides reasoning for Claims 1, 9 and 18 standing as rejected under 35 U.S.C. 102(b) as being anticipated by Heard *et al*. (2004). Briefly, the Heard et al. prior art teaches a method for the treatment of traumatic brain injury in mammals comprising administering recombinant human G-CSF that is 100% identical to that of SEQ ID NO: 28 of the instant claims to human patients with traumatic brain injury. The Heard reference does not teach the method further comprising administering one or more additional hematopoietic factors, nor specifically erythropoietin as required by instant claims 5, 6, and 7, however, the Brine et al. reference, however, teaches that methods for the treatment of traumatic brain injury comprising administering erythropoietin were well-known in the art prior to filing. Thus, the invention is *prima facie* obvious for reasons of record in the Paper mailed May 22, 2008 and the rejection is maintained.

15. Claim 12 stands as rejected under 35 U.S.C. 103(a) as being unpatentable over Heard et al., and further in view of Deleuze (2000) for reasons of record in the Paper mailed May 22, 2008.

On page 8 or Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that because the primary reference, Heard, is silent about treating the underlying condition of TBI, then each of the combinations subsequently fail.

In above sections 10-12 of the instant office action Examiner provides reasoning for Claims 1, 9 and 18 standing as rejected under 35 U.S.C. 102(b) as being anticipated by Heard *et al*. (2004). Briefly, the Heard et al. prior art teaches a method for the treatment of traumatic brain injury in mammals comprising administering recombinant human G-CSF that is 100% identical to that of SEQ ID NO: 28 of the instant claims to human patients with traumatic brain injury. The Heard reference does not teach the method further comprising administering tissue plasminogen activator as required by instant claim 12. The Deleuze reference, however, teaches treatments of traumatic brain injury comprising administration of tissue plasminogen activator were known in the art. Therefore, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference and the rejection is maintained.

16. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heard, and further in view of Morita-Fujimura (1999) for reasons of record in the Paper mailed May 22, 2008.

On page 8 or Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that because the primary reference, Heard, is silent about treating the underlying condition of TBI, then each of the combinations subsequently fail.

In above sections 10-12 of the instant office action Examiner provides reasoning for Claims 1, 9 and 18 standing as rejected under 35 U.S.C. 102(b) as being anticipated by Heard *et al*. (2004). Briefly, the Heard et al. prior art teaches a method for the treatment of traumatic brain injury in mammals comprising administering recombinant

human G-CSF that is 100% identical to that of SEQ ID NO: 28 of the instant claims to human patients with traumatic brain injury. The Heard reference does not teach the method further comprising an anti-apoptotic agent defined within the specification as "e.g. inhibitors of caspases". However, Morita-Fujimura et al. teach the administration of inhibitors of caspases for the treatment of traumatic brain injury in mammals was known in the art prior to filing. Therefore, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference for reasons of record and the rejection is maintained.

17. Claim 16 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Heard, and further in view of Brines et al. and Deleuze et al.

On page 8 or Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that because the primary reference, Heard, is silent about treating the underlying condition of TBI, then each of the combinations subsequently fail.

In above sections 10-12 of the instant office action Examiner provides reasoning for Claims 1, 9 and 18 standing as rejected under 35 U.S.C. 102(b) as being anticipated by Heard *et al*. (2004). Briefly, the Heard et al. prior art teaches a method for the treatment of traumatic brain injury in mammals comprising administering recombinant human G-CSF that is 100% identical to that of SEQ ID NO: 28 of the instant claims to human patients with traumatic brain injury. The Heard reference does not teach the method further comprising administering both erythropoietin and tissue plasminogen activator as required by instant claim 16. However, since each of the elements are

taught by the prior art to be useful for the same purpose of treating traumatic brain injury, then it is *prima facie* obvious to combine the elements into a single composition. Therefore the rejection is maintained.

18. Claims 109 and 110 stand as rejected under 35 U.S.C. 103(a) as being unpatentable over Heard, and further in view of Curran and Goa (2002) for reasons of record in the Paper mailed May 22, 2008.

On page 8 or Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that because the primary reference, Heard, is silent about treating the underlying condition of TBI, then each of the combinations subsequently fail.

In above sections 10-12 of the instant office action Examiner provides reasoning for Claims 1, 9 and 18 standing as rejected under 35 U.S.C. 102(b) as being anticipated by Heard *et al*. (2004). Briefly, the Heard et al. prior art teaches a method for the treatment of traumatic brain injury in mammals comprising administering recombinant human G-CSF that is 100% identical to that of SEQ ID NO: 28 of the instant claims to human patients with traumatic brain injury. The Heard reference does not teach the method further comprising administering a mammalian (human) G-CSF comprising one or more chemical substituents as required by instant claims 109 and 110. The Curran and Goa reference, however, teach that, prior to filing, pegylated filgrastim was known in the art as a substitute for the filgrastim used in the Heard reference and that this chemically substituted version of filgrastim confers specific advantages for

administration to patients. A skilled artisan would have deemed it obvious to combine the teachings of the reference, and the rejection is maintained.

19. Claims 111 and 112 stand as rejected under 35 U.S.C. 103(a) as being unpatentable over Heard, and further in view of MacVittie et al. (2000).

On page 8 or Remarks filed July 24, 2008, Applicant traverses the rejection on the grounds that because the primary reference, Heard, is silent about treating the underlying condition of TBI, then each of the combinations subsequently fail.

In above sections 10-12 of the instant office action Examiner provides reasoning for Claims 1, 9 and 18 standing as rejected under 35 U.S.C. 102(b) as being anticipated by Heard *et al*. (2004). Briefly, the Heard et al. prior art teaches a method for the treatment of traumatic brain injury in mammals comprising administering recombinant human G-CSF that is 100% identical to that of SEQ ID NO: 28 of the instant claims to human patients with traumatic brain injury. The Heard reference does not teach the method further comprising administering a mammalian (human) G-CSF fused to a second protein as required by instant claims 111 and 112. The MacVittie et al., reference, however, teaches that chimeric IL-3/G-CSF fusion proteins, termed Myelopoietins in the art, were known as substitutes for G-CSF prior to filing, and that these Myelopoietins display a more favorable pharmacodynamic profile than G-CSF alone . Therefore, a skilled artisan would have been motivated to combine the teachings and the rejection is maintained because the invention as a whole is prima facie obvious.

New Grounds – Necessitated by Amendment

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. As amended, Claims 105-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heard et al. as applied to claims 1, 9, 18 and 106-108 above, and further in view of Neupogen® (Filgrastim) Amgen product information, published April 2, 1998.

22. As currently amended, Claims 105-112 read upon a method of treating TBI in a mammal comprising intravenously administering G-CSF.

The Heard et al. prior art teaches a method comprising administering recombinant human G-CSF that is 100% identical to that of SEQ ID NO: 28 of the instant claims to human patients with traumatic brain injury. The Heard reference, however, administers GCSF subcutaneously and does not teach the method comprising intravenous administration. The product information published by the maker of commercially available human GCSF, Amgen, prior to filing indicate that Filgrastim could be interchangeably administered by oral, intravenous, subcutaneous, or intraperitoneal routes with no significant difference in effect. In *KSR International Co. v. Teleflex, Inc.,* the Supreme Court has stated that where there is a "pressure to solve a problem and a finite number of identified, predictable solutions, a person of ordinary skill has good

reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense" (*KSR International Co. v. Teleflex, Inc.* 127 S. Ct. 1727, 82 USPQ2d 1385, Supreme Court, April 30, 2007). In the instant case, the problem to be solved is the route of administration and the art demonstrates that there are a finite number of ways to administer and does not indicate any differing effects by either route. Therefore, it would have been obvious to one of ordinary skill in the art to combine the method as taught by Heard et al., with the routes of administration as taught by the product manufacturer. Therefore, the invention as a whole is *prima facie* obvious if not anticipated by the prior art.

Double Patenting

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 1, 5-7, 9, 11-14, 16-19 and 105-112 stand as provisionally rejected over claims 1-5, 9-22 and 52-53 of copending Application No. 10/880,101 for reasons of record in the Paper mailed 1/19/2007.

On page 9 of Remarks file July 24, 2008, Applicant traverses the rejection on the grounds that treating traumatic brain injury is not an obvious variant upon treating peripheral neuropathy and vice versa. This is not found persuasive because the specification of the '101 application explicitly states, "Peripheral neuropathy is a pain initiated or caused by a primary lesion or dysfunction of the nervous system … The causes of neuralgia include direct trauma, penetrating injuries" [0053]. Therefore the provisional rejection is maintained.

Conclusion

25. No Claim is allowed.

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M,W and ALT F 7 am to 3:30, T & R 5:30 -5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane

Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649